

In the Claims:

Claims 11 to 23 have been cancelled.

Claims 1 and 3 have been amended as follows:

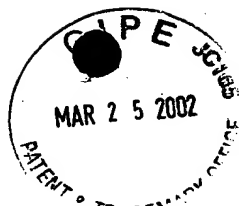
1. (Twice Amended) An isolated and purified nucleic acid molecule having a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence consisting of [set forth in Figure 3, 4 or 5 (SEQ ID Nos: 5, 6, 8[,] or 10)] for *Moraxella catarrhalis* strains 4223, Q8 and LES-1 respectively] or the complementary sequence thereto,
- (b) a nucleotide sequence encoding an about 200 kDa outer membrane protein of a strain of *Moraxella catarrhalis* and consisting of [having the derived amino acid sequence shown in Figures 3, 4 or 5 (SEQ ID Nos: 7, 9[,] or 11)] for *Moraxella catarrhalis* strains 4223, Q8 and LES-1 respectively], and
- (c) a nucleotide sequence encoding an about 200 kDa outer membrane protein of another strain of *Moraxella catarrhalis* which is characterized by a tract of consecutive G nucleotides which is 3 or a multiple thereof in length, an ATG start codon about 80 to 90 bp upstream of said tract and said tract being located between about amino acids 25 and 35 encoded by the nucleotide sequence.

3. (Amended) An isolated and purified nucleic acid molecule having a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence consisting of [set forth in Figure 8 (SEQ ID No: 12)] for a 5'-truncation of the gene encoding an about 200 kDa outer membrane protein of *Moraxella catarrhalis* strain 4223],
- (b) a nucleotide sequence encoding the derived amino acid sequence consisting of [set forth in Figure 9 (SEQ ID No: 13)] for a N-terminal truncation of an about 200 kDa outer membrane protein of *Moraxella catarrhalis* strain 4223], and
- (c) a nucleotide sequence encoding a 5'-truncation of a gene encoding an about 200 kDa outer membrane protein of another strain of *Moraxella catarrhalis* and which expresses [being capable of expressing] the

corresponding N-terminally truncated about 200 kDa outer membrane protein from *E. coli*.



Allowed claims in 08/431,718 (Now USP 6,335,018)

1. An isolated and purified outer membrane protein of a *Moraxella catarrhalis* strain having an apparent molecular mass of about 200 kDa, as determined by SDS-PAGE.
3. The protein of claim 1 wherein the strain is *Moraxella catarrhalis* 4223 or RH408.
4. The protein of claim 1 containing the amino acid sequence NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-x-Gln-Gly-Ile (SEQ ID NO:2) for the *Moraxella catarrhalis* strain 4223.
5. The protein of claim 1 which is at least about 70 wt% pure.
6. The protein of claim 5 which is at least about 95 wt% pure.
7. The protein of claim 1 in the form of an aqueous solution thereof.
8. The protein of claim 1 recognizable by an antibody preparation specific for a peptide having the amino acid sequence of NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-x-Gln-Gly-Ile (SEQ ID NO:2).
20. A recombinant outer membrane protein of a *Moraxella catarrhalis* strain having an apparent molecular mass of about 200 kDa as determined by SDS-PAGE producible by a transformed host containing an expression vector comprising a nucleic acid sequence which is:
  - (A) a purified and isolated nucleic acid molecule encoding an outer membrane protein of a strain of *Moraxella catarrhalis* having a molecular mass of about 200 kDa, as determined by SDS-PAGE, or
  - (B) a purified and isolated nucleic acid molecule having a sequence selected from the group consisting of:
    - (a) the nucleotide sequence set out in Figure 6 (SEQ ID NO:1) or the complementary sequence thereto,
    - (b) a nucleotide sequence encoding a 200 kDa protein of a strain of *Moraxella catarrhalis* and containing the amino acid sequence NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-x-Gln-Gly-Ile (SEQ ID NO:2); and
    - (c) a nucleotide sequence encoding a 200 kDa portion of a strain of *Moraxella catarrhalis* and which hybridizes under

stringent conditions to any one of the sequences defined in (a) or (b); and

expression means operatively coupled to the nucleic acid molecule for expression by the host of the 200 kDa outer membrane protein of *Moraxella catarrhalis*.

23. A peptide having no less than six amino acids and no more than 150 amino acids and containing an amino acid sequence corresponding to a portion only of an outer membrane protein of a strain of *Moraxella catarrhalis* having a molecular mass of about 200 kDa, as determined by SDS-PAGE, said peptide having the amino acid sequence NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-x-Gln-Gly-Ile (SEQ ID No: 2) or NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys (SEQ ID No: 3) for the *Moraxella catarrhalis* 4223 strain.

10. A purified and isolated nucleic acid molecule encoding an outer membrane protein of a strain of *Moraxella catarrhalis* having a molecular mass of about 200 kDa, as determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis.
12. The nucleic acid molecule of claim 10, wherein the strain is *Moraxella catarrhalis* 4223.
13. The nucleic acid molecule of claim 10, wherein the encoded protein contains the amino acid sequence NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-Lys-Gln-Gly-Ile (SEQ ID No: 8) for *Moraxella catarrhalis* strain 4223 or contains the corresponding amino acid sequence from other *Moraxella catarrhalis* strains.
14. A purified and isolated nucleic acid molecule having a sequence selected from the group consisting of:
  - (a) a DNA sequence as set out in Figure 6 (SEQ ID No: 2), or the complementary sequence thereto;
  - (b) a DNA sequence encoding an about 200 kDa protein of a strain of *Moraxella catarrhalis* and containing the amino acid sequence NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-Lys-Gln-Gly-Ile (SEQ ID No: 8), or the complementary sequence thereto;
  - (c) a DNA sequence encoding a deduced amino acid sequence as set out in Figure 6 (SEQ ID No: 3), or the complementary sequence to the DNA sequence; and
  - (d) a nucleotide sequence encoding an about 200 kDa protein of a strain of *Moraxella catarrhalis* and which hybridizes under stringent conditions to any one of the DNA sequences defined in (a), (b) or (c).
15. The nucleic acid molecule of claim 14, wherein the nucleotide sequence defined in (d) has at least about 90% sequence identity with any one of the sequences defined in (a), (b) or (c).
16. A vector adapted for transformation of a host comprising the nucleic acid molecule of claim 10 or 14.
17. An expression vector adapted for transformation of a host comprising the nucleic acid molecule of claim 10 or 14 and expression means operatively coupled to

the nucleic acid molecule for expression by the host of said outer membrane protein of a strain of *Moraxella catarrhalis*.

18. The expression vector of claim 17, wherein the expression means includes a nucleic acid portion encoding a leader sequence for secretion from the host of the outer membrane protein.

19. The expression vector of claim 17, wherein the expression means includes a nucleic acid portion encoding a lipidation signal for expression from the host of a lipidated form of the outer membrane protein.

20. A transformed host containing an expression vector as claimed in claim 17.

21. A recombinant outer membrane protein or an immunogenic fragment thereof producible by the transformed host of claim 20.

22. A live vector for delivery of an outer membrane protein of a strain of *Moraxella catarrhalis* having a molecular weight of about 200 kDa to a host, comprising a vector containing the nucleic acid molecule of claim 10 or 14.

23. The live vector of claim 21, wherein the vector is selected from the group consisting of *E. coli*, *Salmonella*, *Mycobacteria*, adenovirus, poxvirus, vaccinia and poliovirus.

Pending claims in 08/483,855 (1038-503)

27. An immunogenic composition, comprising at least one active component selected from the group consisting of:

(A) an isolated and purified outer membrane protein of a strain of *Moraxella catarrhalis* having a molecular mass of about 200 kDa, as determined by SDS-PAGE; and

(B) a peptide having the amino acid sequence NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys-x-Gln-Gly-Ile (SEQ ID No: 2) or NH<sub>2</sub>-Asn-Val-Lys-Ser-Val-Ile-Asn-Lys-Glu-Gln-Val-Asn-Asp-Ala-Asn-Lys (SEQ ID No: 3); and a pharmaceutically acceptable carrier therefor, said at least one active component producing an immune response when administered to a host.

30. The immunogenic composition of claim 27 formulated as a microparticle, capsule, ISCOM, or liposome preparation.

31. The immunogenic composition of claim 27 in combination with a targeting molecule for delivery to specific cells of the immune system or to mucosal surfaces.

32. The immunogenic composition of claim 27 further comprising at least one other immunogenic or immunostimulating material.

33. The immunogenic composition of claim 32 wherein the at least one other immunostimulating material is at least one adjuvant.

34. The immunogenic composition of claim 33 wherein the at least one adjuvant is selected from the group consisting of aluminum phosphate, aluminum hydroxide, QS21, Quil A, calcium phosphate, calcium hydroxide, zinc hydroxide, a glycolipid analog, an octodecyl ester of an amino acid, a muramyl dipeptide and a lipoprotein.

35. The immunogenic composition of claim 34 wherein the host is a primate.

36. The immunogenic composition of claim 35 wherein the primate is a human.

38. A method of generating an immune response in a host, comprising administering thereto an immuno-effective amount of the immunogenic composition of claim 27.

39. The method of claim 38 wherein the immune response is a humoral or a cell-mediated immune response.

49. A method of producing an isolated and purified outer membrane protein of a strain of *Moraxella catarrhalis* having a molecular mass of about 200 kDa, as determined by SDS-PAGE, comprising the steps of:

- (a) providing a cell mass of the *Moraxella catarrhalis* strain;
- (b) disrupting the cell mass to provide a cell lysate;
- (c) fractionating the cell lysate to provide a fraction containing the outer membrane protein substantially free from other cell lysate components, and
- (d) recovering said outer membrane protein.

50. The method of claim 49 wherein said *Moraxella catarrhalis* strain is *Moraxella catarrhalis* strain 4223.

51. The method of claim 50 wherein the cell lysate is fractionated by gel electrophoresis.



Pending Claims in 08/621,944 (1038-587)

1. An isolated and purified outer membrane protein of a *Moraxella catarrhalis* strain having an apparent molecular mass of about 200 kDa, as determined by SDS-PAGE, characterized by an amino acid sequence selected from the group consisting of:
  - (a) an amino acid sequence containing SEQ ID NO:3;
  - (b) an amino acid sequence encoded by SEQ ID NO:1 or 2;
  - (c) an amino acid sequence containing SEQ ID NO:8;
  - (d) an amino acid sequence containing an amino acid sequence encoded by SEQ ID NO:7;
  - (e) an amino acid sequence containing SEQ ID NO:6;
  - (f) an amino acid sequence containing SEQ ID NO:9; and
  - (g) an amino acid sequence containing SEQ ID NO:10.
5. The protein of claim 1 which is at least about 70 wt.% pure.
6. The protein of claim 5 which is at least about 95 wt.% pure.
7. The protein of claim 1 in the form of an aqueous solution thereof.
9. The protein of claim 1 having the amino acid composition as shown in Table III.
24. A peptide consisting of an amino acid sequence selected from the group consisting of SEQ ID NO:9 and SEQ ID NO:10.